MTN-004

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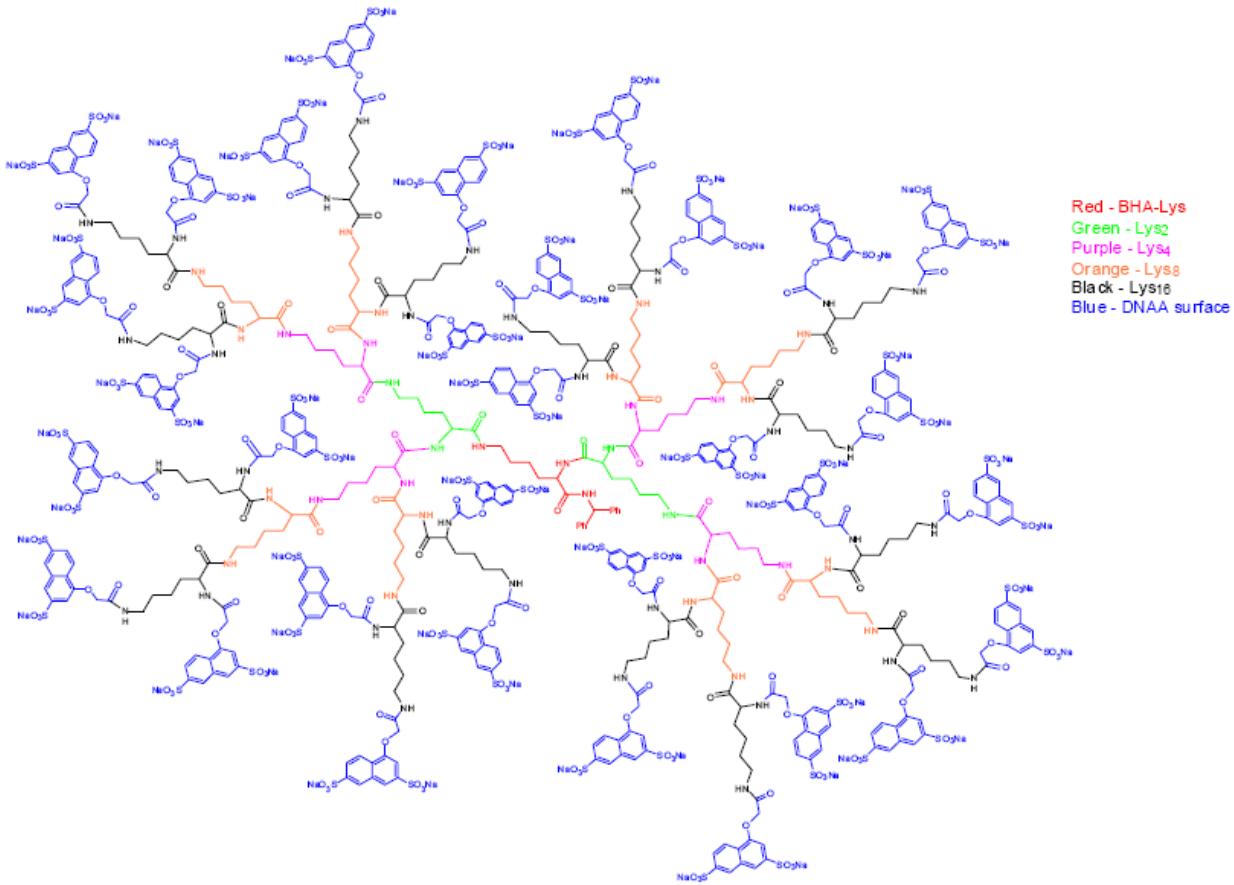
SPL7013 (VivaGel™)



SPL7013 (VivaGel™)

- Polylysine dendrimer molecule with 32 copies of naphthalene-3, 6-disulfonate
- In vitro activity activity against HSV-2 and HIV-1
- INDs filed for both indications
- Completed Phase 1 study (0.5% - 3% w/w SPL7013) seven doses
- Ongoing Phase 1 study under STI-CTG auspices in San Francisco and Kisumu, Kenya
- Phase 1 rectal safety study in planning stage

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- Phase 1, double blind, randomized, controlled comparison with 14 days of twice daily exposure to 3% w/w SPL7103 Gel or placebo gel in HIV-uninfected sexually active women

Arm	Description	N	Frequency
1	SPL7013 Gel	20	BID (14 days)
2	Placebo Gel	20	BID (14 days)

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Primary Objective

- To assess the safety of 3% w/w SPL7013 Gel when administered for 14 consecutive days on the vulvar and cervicovaginal mucosa of healthy sexually active HIV-negative women aged 18-24 years

Secondary Objectives

- To assess the **adherence** to a short-term regimen of 3% w/w SPL7013 Gel among healthy sexually-active HIV-negative women aged 18-24 years
- To evaluate product **acceptability** among healthy sexually-active HIV-negative women aged 18-24 years
- To assess the effect of a twice daily short-term regimen of 3% w/w SPL7013 Gel on the **vaginal microflora** of healthy sexually-active HIV-negative women aged 18-24 years

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Exploratory Objectives

- Determine the pattern of cytokine/chemokine, innate immune factor changes, and functional activity associated with use of 3% w/w SPL7013 Gel in the lower reproductive tract of healthy sexually active HIV-negative women aged 18 – 24 years.
- Determine by means of dye-based applicator test the number of applicators returned to the study site that have been exposed to the vagina
- Determine the extent of SPL7013 absorption into the blood following the completion of product dosing

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Primary Endpoints

- Abnormal genital symptoms judged by the Investigator to be possibly, probably, or definitely related to product use
- Abnormal pelvic exam findings, including colposcopic findings, judged by the Investigator to be possibly, probably, or definitely related to product use
- Grade 3 or higher laboratory values (as defined by the DAIDS Toxicity Tables) for hematology, liver function, creatinine level and coagulation judged by the Investigator to be possibly, probably, or definitely related to product use
- Adverse experiences judged by the Investigator to be possibly, probably, or definitely related to product use

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MTN-004 Study Design

Activity	Screen 1	Screen 2	Enroll	Phone Call (D2)	Week 1	Week 2	Week 3
Consent							
Screening	X	(X)					
Safety bloods	X	(X)	X		X	X	
Pelvic exam			X		X	X	X
Colposcopy			X			X	
PK			X			X	
Behavioral			X			X	
Vag culture			X		X	X	X
Innate factors			X		X	X	X

MTN-004 Sites

Student Health Center
University of South Florida
Tampa, Florida
Site PI: Diane Straub MD MPH

Maternal Infant Study Center (CEMI)
University of Puerto Rico
Medical Science Campus
San Juan, Puerto Rico
Site PI: Irma Febo MD

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Innovative Aspects of MTN-004

- Collaboration between
  - DAIDS & NICHD
  - MTN & ATN
- Behavioral Sub study
  - Web based assessments
  - Daily cell phone driven questionnaires
- Innate immunity assessment
  - Cervical cytokines
  - Innate immune factors (SLPI and lactoferrin)
  - Functional activity (antibacterial and antiviral)
- Adherence assessment
  - Applicator dye test

MTN-004 Timelines

Activity	Due Date	Status
Protocol development	November 2006	Completed
PSRC Review	December 2006	Completed
Response to PSRC	December 2006	Completed
Protocol sign off by DAIDS MO	December 2006	Completed
IRB Submission & approval	January 2007	Completed
Protocol Registration	April 2007	Pending
Screening and enrollment	April/May 2007	Pending
Study completion	November 2007	Pending

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